News and Resources from the National Institutes of Health

Digestive Diseases
NEWS
National Digestive Diseases Information Clearinghouse
Spring 2006

Celiac Disease 'Greatly Underdiagnosed,' Says NIH Consensus Panel

NIDDK to Launch Campaign to Boost Physician Understanding

Hundreds of thousands of patients with celiac disease remain undiagnosed, an independent consensus panel convened by the National Institutes of Health (NIH) has concluded. The panel recommended that doctors think about celiac disease as a possible diagnosis when considering the origin of a wide range of symptoms, from short stature to abdominal pain to fatigue.

The panel concluded that as many as 1 percent of all Americans suffer from celiac disease, more than previously thought. Many of those people, however, have never received a diagnosis of celiac disease and are not being treated.

"The main point is that celiac disease is grossly underdiagnosed, and it is much more common than physicians appreciate," said Charles Elson, M.D., University of Alabama at Birmingham and chair of the consensus panel.

Effective Treatment Exists

Celiac disease is caused by an immune response to gluten in certain grains, and an effective treatment—a gluten-free diet—offers most patients relief from the damage and symptoms. Still, Elson said many physicians do not test for the disease, often leading to a long gap between the onset of symptoms and the diagnosis of celiac disease.

Diagnosis rates have further been depressed, Elson said, because of the array of symptoms linked to celiac disease. Though many patients complain of gastrointestinal problems—the traditional presentation of the disease—those with other symptoms may be overlooked. "We are missing it," said

Elson, "and the reason is that celiac disease does not always present with the classic symptoms. Some people are presenting with gastrointestinal issues, but others are not."

Awareness Campaign Prepared

In response to the panel's recommendations, the NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is preparing to launch a physician-directed awareness campaign to emphasize disparate disease presentations, testing, and dietary interventions. "Heightened

Celiac Disease, continued on page 2

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National Institute of Diabetes and Digestive and Kidney Diseases

Celiac Disease, from page 1

The consensus panel developed a six-point recommendation for management of patients who have received a diagnosis of celiac disease:

- **C** – Consultation with a skilled dietitian
- **E** – Education about the disease
- **L** – Lifelong adherence to a gluten-free diet
- **I** – Identification and treatment of nutritional deficiencies
- **A** – Access to advocacy groups
- **C** – Continuous long-term follow-up

awareness of this disease is imperative," the consensus panel report concluded. "Education of physicians, registered dietitians, and other health providers is needed."

The 13-member panel's report followed 2 days of extensive discussions and testimony from experts about the disease, its diagnosis, and treatment.

In addition to pushing doctors to more aggressively evaluate patients for celiac disease, the consensus panel called for efforts to refine the criteria by which the disease is diagnosed, better define what constitutes a "gluten-free diet," improve testing of food for traces of gluten, and form a federation of interested groups that can work together to improve education and research.

Though the treatment for celiac disease is well defined, the members of the consensus panel also created an extensive list of research priorities for the study of celiac disease, ranging from better data about the prevalence of the disease in specific populations to alternatives to the gluten-free diet and improved understanding of the link between celiac disease and other health problems. ■

Digestive Diseases News Gets a New Look

Digestive Diseases News has received a facelift. Longtime subscribers to the newsletter may have noticed some changes, both in look and content, in this issue of *Digestive Diseases News*. We redesigned the publication with an eye toward making it more readable and better tailored to the needs of subscribers.

Readers will also see the publication more often. *Digestive Diseases News* has traditionally been published twice a year. We now plan to produce the newsletter quarterly, bringing readers fresher news about the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

The new layout is intended to make navigating the publication simpler. The front page has been designed to highlight each issue's main topic. The top of each page now highlights the featured topic, making it simple to separate research news from the list of updated publications.

But the changes go beyond the cosmetic. Though *Digestive Diseases News* will continue its focus on reporting the latest in NIDDK news and updates from the National Digestive Diseases Information Clearinghouse, we will also search for stories about the most interesting people and projects at the agency.

Our effort to produce the highest quality, most interesting publication requires the help of our readers. If you know of stories *Digestive Diseases News* should be chasing or profiles it should be running, please contact the newsletter staff at 703–902–1302. ■

Digestive Diseases
NEWS

Digestive Diseases News is published four times a year by the National Digestive Diseases Information Clearinghouse (NDDIC). The newsletter features news about digestive diseases, special events, patient and professional meetings, and new publications available from the NDDIC and other related organizations.

Subscriptions are free but available only to health professionals. Send subscription inquiries to: National Digestive Diseases Information Clearinghouse, 2 Information Way, Bethesda, MD 20892–3570. This publication is also available online at *www.digestive.niddk.nih.gov/about/newsletter.htm*.

Camps for Children With Celiac Disease Prove Popular

Demand for Summer Programs Increases Across the Country

At first glance, Camp Celiac has all the elements of a traditional summer camp. A lush forest. A sparkling pond. Rustic cabins. But what makes the week-long getaway extraordinary is what the camp lacks—gluten.

Set in rural Rhode Island, Camp Celiac will celebrate 7 years of operation this coming summer. Growing from a weekend outing for a few dozen children, Camp Celiac is now a full-blown camp serving more than 120 children, including its first overseas camper from Sweden.

"These kids come to camp and say 'Can we eat this?' 'Can we eat that?' After 24 hours they catch on that they can eat anything they want."

Tanis Collard
Camp Celiac director

"It has exploded into this huge venture," said Tanis Collard, Camp Celiac's director, who founded the modest weekend event 6 years ago to help her daughter find other children facing the same dietary challenges. "I started the camp as a weekend sleep-away camp for children with celiac disease in the hopes that my daughter would meet some kids like her. That weekend about 50 campers came. At the end of that weekend, the kids begged us to do more."

Gluten-Free Kitchen

Collard said the entirely gluten-free kitchen comes as the biggest shock to new attendees who sometimes have a hard time wrapping their minds around it. "These kids come to camp and say 'Can we eat this?' 'Can we eat that?' After 24 hours they catch on that they can eat anything they want. It's really kind of funny."

Ensuring the camp is free of wheat, barley, and rye—the grains that trigger the immune system reaction that causes the intestinal symptoms of celiac disease—is the simple part, said Collard. The cook at Camp Aldersgate, where the camp is hosted, was willing to learn the ins and outs of gluten-free cooking. Now, the real challenge is entertaining a camp full of children for a week.

A Growing Trend

Camp experiences for children with celiac disease have been around for at least 2 decades. The Gluten Intolerance Group (GIG) has helped gluten-free campers find spots at Seattle-area camps since 1987, and interest is still growing.

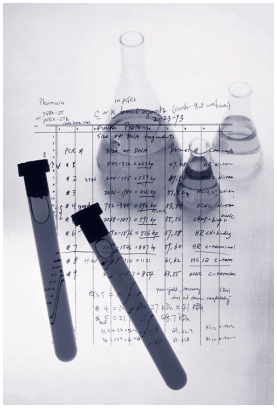
In addition to Camp Celiac and the GIG's efforts at Camp Sealth in Seattle, there are now spots for children with celiac disease at a North Carolina camp that is working with the GIG, a long weekend at Camp Oh-Da-Go-Ta in Wisconsin, and the Great Gluten Escape in Texas.

Unlike Camp Celiac, the camps supported by the GIG serve a broad population of children, with celiac disease campers accounting for approximately 10 percent of the 350 campers at Camp Sealth. The GIG runs a separate kitchen to serve the needs of the campers who cannot tolerate gluten, which allows children with celiac disease to fully participate in camp life.

"You don't live in a bubble, so we try to teach them to be a part of everyday life," said Cynthia Kupper, executive director of the GIG. "It gives us an opportunity to educate the campers and the staff."

Kupper said the education mission appears to be working. Last year, one cabin decided to eat entirely gluten-free to support their gluten-free campmate.

There is little risk of the camps for children with celiac disease disappearing. Kupper said the GIG is looking into supporting campers who have both celiac disease and diabetes—an increasingly common population—and Collard said her 12-year-old daughter has implored her to continue her volunteer efforts. But that lobbying may be unnecessary, Collard said. "You look at these kids' faces and you know that you have to do it again." ■



Five Centers Examining Drug-Liver Damage Link

NIDDK Program Searches for Mechanisms Behind Adverse Events

Drug-induced liver injury has been a clinical issue for years, as doctors, regulators, and researchers struggle to determine what therapeutics might damage the organ. Now, an ambitious network funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is beginning to tease out information about how drugs damage the liver.

One of the goals of the network is to build the knowledge base for understanding which patients are at risk, not simply what drugs are implicated.

Established 2 years ago, the Drug Induced Liver Injury Network (DILIN) seeks to understand the mechanism of liver toxicity and to identify strategies to prevent adverse events in patients taking prescription drugs.

Two Studies Underway

The five-center network has begun two research studies. One retrospective study looks at patients who have at any time since 1994 suffered an injury after taking at least one of four different drugs known to have deleterious effects on the liver. The other seeks to recruit patients who have recently suffered a potentially severe liver injury due to drugs.

"The most important goals that the DILIN will accomplish are to establish and validate new causality instruments and collect specimens and a comprehensive database about cases that are due to drug-induced liver injury," said José Serrano, M.D., Ph.D., who directs the network at the NIDDK. "It will become a tremendous resource that will allow the testing of hypotheses on the mechanism of injury."

The network receives $2.25 million a year to conduct the research.

Reactions to Four Drugs Examined

The retrospective study examining past liver injuries targets reactions to four drugs: the tuberculosis treatment isoniazid; phenyton and valproic acid, which are seizure medications; and the popular antibiotic combination of amoxicillin and clavulanate, sold as Augmentin.

The two protocols have already enrolled more than 200 patients, an effort Serrano called "quite successful." In addition to getting details about the clinical course of liver disease in those patients, researchers collect blood and other biological samples, allowing future detailed biologic and genetic analysis of the patients. The data is publicly available through the NIDDK.

The Five DILIN Centers

- University of Connecticut at Hartford
- Indiana University at Indianapolis
- University of California at San Francisco
- University of Michigan at Ann Arbor
- University of North Carolina at Chapel Hill

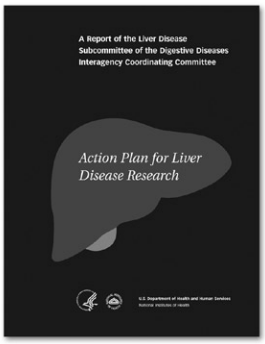
Little Known about How Damage Occurs

Despite the high-profile adverse events, Serrano said researchers still know little about how such damage occurs, in part because reactions are rare and difficult to diagnose, making it harder to analyze trends. One goal of the network is building a knowledge base for understanding which patients are at risk, not simply what drugs are implicated.

"Overall, we believe that the DILIN will bring greater focus and interest to the study of drug-induced liver injury and help develop better ways to prevent, detect, and treat this growing liver problem," said Paul Watkins, M.D., chair of the DILIN steering committee and the principal investigator at the University of North Carolina at Chapel Hill, one of the DILIN centers. ■

'Action Plan' Outlines Coordinated Research Approach to Combatting Liver Disease

The National Institutes of Health (NIH) has brought together several of its Institutes, Centers, and Offices to map out a comprehensive strategy to guide future research about liver disease.



"The explosion of knowledge about fundamental biology and genetics in the past 20 years now promises to provide significant improvements in the management of liver disease."

Jay Hoofnagle, M.D.
NIDDK director of the Liver Disease Research Branch

The effort, detailed in a publication called the *Action Plan for Liver Disease Research*, seeks to boost the rate at which basic scientific discoveries are made and then transformed into clinical breakthroughs that benefit patients. The report called for closer coordination across the NIH and other federal agencies and set 214 research goals in more than a dozen categories.

"The major focus of this Action Plan is to stimulate translation of basic research findings into practical and effective means of prevention and control of liver diseases," said Jay Hoofnagle, M.D., director of the Liver Disease Research Branch at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), which funds 39 percent of all the NIH liver disease research.

'Explosion of Knowledge'

"The explosion of knowledge about fundamental biology and genetics in the past 20 years now promises to provide significant improvements in the management of liver disease," Hoofnagle said.

Among the Institutes joining the NIDDK in the development of the plan are the National Institute of Allergy and Infectious Diseases, which funds 18 percent of the NIH liver research, the National Cancer Institute, which pays for 16 percent of such work, and the National Institute on Alcohol Abuse and Alcoholism, which funds 9 percent.

Funding for liver disease has been one of the fastest-growing areas of medical research-related support, tripling in the past decade and outstripping the increase in the overall NIH budget as additional resources have been brought to bear on diseases ranging from liver cancer to hepatitis to cirrhosis. Almost $400 million was spent on liver disease research in 2003.

Focus on Translational Research

In consultation with more than 250 experts, including researchers, physicians, and representatives of professional and patient advocacy groups, the NIDDK's Liver Disease Research Branch and the Liver Disease Subcommittee of the Digestive Diseases Interagency Coordinating Committee developed the Action Plan with a special focus on translational research (see story page 6). Such research is a central element of the NIH's strategic plan—the "NIH Roadmap for Medical Research in the 21st Century." The Roadmap seeks to efficiently bridge the gap between basic research and therapies—diagnostics—for patients.

The Action Plan highlights several other principles designed to guide liver research. "These principles are axiomatic," the report states, "but have been found to be reliable in guiding initiatives in biomedical research." In addition to the push for translational research, the guiding principles include a commitment to basic research, an effort to ensure that new findings at the clinical level help to inform more fundamental research, and an emphasis on fully utilizing important breakthroughs in other fields such as the Human Genome Project.

The document also announces plans to tackle several specific projects as representative "benchmarks" for assessing the overall success of the Action Plan, calling for ways to improve the success rate of hepatitis C therapy, to find better ways of measuring liver fibrosis, and to improve liver cancer screening. ■

Seven Initiatives Seek to Bridge Basic, Clinical Research

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is pushing to improve the ability of researchers to turn breakthroughs in basic science into new patient treatments and tests, focusing its attention on several initiatives designed to promote this translational research.

The effort to boost translational research follows a high-profile 2003 call to action by participants in the Institute of Medicine's Clinical Research Roundtable. Those researchers, writing in the *Journal of the American Medical Association*, said they were worried that scientific breakthroughs "are failing to be translated efficiently into tangible human benefit."

Part of NIH Roadmap

The National Institutes of Health (NIH) has made promotion of translational research a centerpiece of its "Roadmap for Medical Research in the 21st Century," and the NIDDK will concentrate its resources in seven areas, including better imaging technologies, better animal models, and a more vigorous search for drugs to treat diseases caused by misformed proteins.

"Concrete initiatives are coming out of this," said Allen Spiegel, M.D., former director of the NIDDK, who said the effort is designed to help fill "valleys of support" in the research spectrum.

Spiegel acknowledged that the move toward more robust translational research at the NIH will require partnerships with industry, such as pharmaceutical companies, which often foots the bill for later-stage research. "If we are to be successful in translational research, we will have to be extremely thoughtful in how we deal with industry." ■

The Seven Translational Areas

- **Biomarkers:** The NIDDK is encouraging researchers to examine new ways to assess disease progression and treatment effects through the use of new tests using blood, tissue, and other samples.
- **Imaging of Solid Abdominal Organs and the Urinary Tract:** Doctors are often frustrated by the lack of reliable noninvasive ways of monitoring digestive, kidney, and urinary health, prompting an effort to find better imaging technology and techniques that will allow physicians a more precise understanding of these diseases.
- **Animal Models:** The NIDDK is pushing researchers to work on finding new or improved animal models in an effort to improve the safety and efficacy testing of new therapies that must be done before a treatment is offered to humans.
- **Angiogenesis and Diabetes:** Control of angiogenesis—the process by which the body creates new blood vessels—could lead to better understanding of several complications of diabetes, such as wound healing and nerve damage, and research into this process may improve the outcomes of islet transplant in patients with type 1 diabetes.
- **Preventing Oxidative Stress:** Hyperglycemia, or high blood glucose, often causes a buildup of damaging oxygen molecules in a part of the cell called the mitochondria. The NIDDK is encouraging researchers to find new ways to halt that process, and thereby lessen complications from diabetes.
- **New Therapies Targeting Proteins:** Errors in the way proteins are made and used in the body are responsible for a range of diseases; this effort seeks to find molecules capable of stopping those defects.
- **RNA Interference:** The NIH would like researchers to realize the promise of therapies that interfere with messenger RNA molecules responsible for disease processes, an early-stage research effort that has generated many unresolved issues.

NIDDK Welcomes Five New Members to Advisory Council

Five new members have been named to the Advisory Council of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The body serves both to guide the NIDDK's discussion of broad science policy issues and to provide second-level review of funding requests. The new members, who will serve until 2009, are:

David M. Klurfeld, Ph.D.: Klurfeld serves the U.S. Department of Agriculture as a national program leader in human nutrition in the Agricultural Research Service, where he oversees research designed to define the role of food and its constituents in optimizing health. Klurfeld will join the Digestive Diseases and Nutrition Subcommittee.

From left to right: David H. Perlmutter, M.D., David M. Klurfeld, Ph.D., Juanita Lynne Merchant, M.D., Ph.D., Mitchell A. Lazar, M.D., Ph.D., Griffin P. Rodgers, M.D., Acting Director, NIDDK, and Margery Deutz Perry. Photo credit: NIDDK.

Mitchell A. Lazar, M.D., Ph.D.: Lazar is a Sylvan H. Eisnman Professor of Medicine and Genetics and chief of the division of endocrinology, diabetes, and metabolism at the University of Pennsylvania School of Medicine in Philadelphia, and he directs the Institute for Diabetes, Obesity, and Metabolism at the Hospital of the University of Pennsylvania in Philadelphia. Lazar joins the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee.

Juanita Lynne Merchant, M.D., Ph.D.: A professor of internal medicine and molecular and integrative physiology at the University of Michigan, Merchant studies how bacterial colonization in the gastrointestinal tract can lead to ulcers and cancer. She joins the Digestive Diseases and Nutrition Subcommittee.

David H. Perlmutter, M.D.: Perlmutter is the Vira I. Heinz Professor and Chair of Pediatrics and a professor of cell biology and physiology at the University of Pittsburgh School of Medicine, the scientific director of the John G. Rangos Sr. Research Center, and physician-in-chief at Children's Hospital of Pittsburgh. Perlmutter studies liver disease and will join the Digestive Diseases and Nutrition Subcommittee.

Margery Deutz Perry: The past chair of research at the Juvenile Diabetes Research Foundation (JDRF) International, Perry oversaw both the development and implementation of the JDRF's research goals and priorities. In addition, she supervised and approved all aspects of the JDRF's research programs. Perry joins the Diabetes, Endocrinology, and Metabolic Diseases Subcommittee.

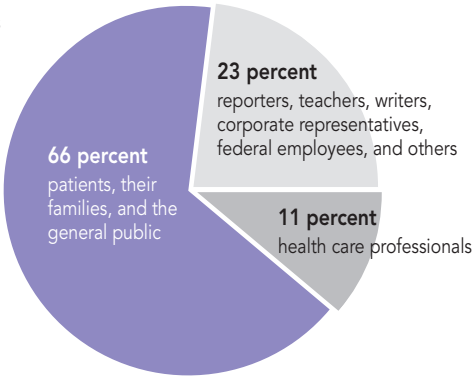
Facts About Inquiry Response June 2004 to April 2005

Clearinghouse Handles More than 6,000 Inquiries, Most from Patients and Families

The National Digestive Diseases Information Clearinghouse responded to 6,072 inquiries between June 1, 2004, and April 30, 2005, according to this breakdown:

Amount	Inquiry Method
2,350	email messages
1,707	telephone calls
1,125	online publication orders
637	mailed letters
181	faxes
72	conferences

Most of those inquiries were from patients and their families:



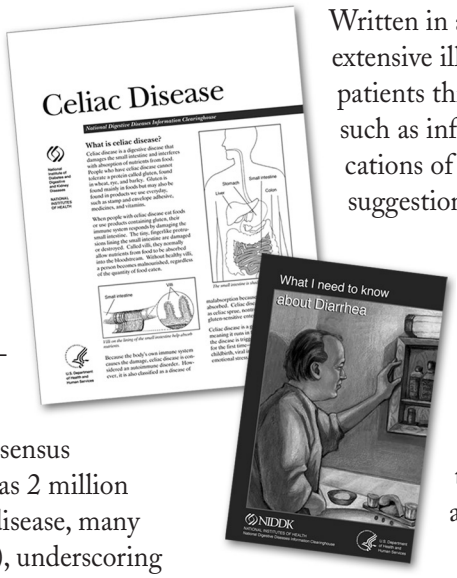
New From NDDIC:

Celiac Disease

As part of the National Digestive Diseases Information Clearinghouse's celiac disease awareness effort, *Celiac Disease* provides health care providers and patients a fact sheet detailing the diagnosis and treatment of the immune disorder.

To order, please call 1–800–891–5389 or visit *www.digestive.niddk.nih.gov*.

The 12-page fact sheet outlines the diagnostic process for celiac disease, focusing on symptoms of the disorder, available screening tools, and information about the best available treatment—a gluten-free diet. The publication offers patients tips for living with the disease and gives educators an additional tool.



A recently convened NIH consensus panel concluded that as many as 2 million Americans suffer from celiac disease, many undiagnosed (see story page 1), underscoring the importance of educational materials at both low- and high-literacy levels.

What I need to know about Diarrhea

What I need to know about Diarrhea, a new easy-to-read publication from the National Digestive Diseases Information Clearinghouse, offers readers a simple guide to diarrhea, one of the most commonly reported illnesses in the United States.

Written in an easy-to-follow format with extensive illustrations, the booklet guides patients through the symptoms, causes—such as infectious disease—and complications of diarrhea and offers treatment suggestions for both adults and children.

In addition, the booklet provides a list of symptoms that should prompt patients to seek care from a health care professional, helping readers distinguish mild cases from those that require medical attention. ■

To order additional copies of this newsletter, or to subscribe to future issues of *Digestive Diseases News*, please visit the NIDDK Information Clearinghouses' online catalog at *www.catalog.niddk.nih.gov*.

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NIH Publication No. 06–4552
May 2006